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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,993	10/13/2000	Shaw-Fen Sylvia Hu	A-357C	2749

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US Patent Operations DRC
Dept. 4300/MS 27-4-A
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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

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11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/687,993	Hu
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 29, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *31 and 45* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *31 and 45* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *31 and 45* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because 37 CFR 1.821 (a)(2)(d) states that each sequence disclosed must appear separately in the "Sequence listing", and referenced appropriately *in the text of the description* and the claims. See MPEP 2422 & 2431. For example, new SEQ ID NO: 51 is not described within the specification on page 5, in contrast to Applicant's assertions. In other words, pages 5 (lines 17, 18 & 19), 7 (line 35), 8 (line 2), 11 (lines 16 & 35) and 20 (lines 2 & 3) need to be amended to list the sequences being discussed. The appropriate statement concerning no new matter and that the CFR and paper copy are identical is also required. Note that any response not placing this application in compliance with the SEQUENCE RULES will be held as non-responsive.

2. The amendment filed 7/29/03 has been entered.

3. Applicants' arguments filed 7/29/03 have been considered but are not found persuasive.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This application contains nonelected SEQ ID NOs: 3-17, 19-38 & new SEQ ID NO:51 in base claim 31, drawn to an invention nonelected with traverse in Paper No. 5. A *complete reply to the final rejection* must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Note that new SEQ ID NO:51 in claim 31 would be rejected as constituting new matter, if it was not withdrawn as a nonelected invention.

6. Claims 31 & 45 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue on page 6 of the response that they have amended the specification as suggested by the Examiner, as it relates to now reciting "consisting of". Therefore, this part of the rejection is obviated. However, the claims still recite "variants", which do not have sufficient written description, especially as it relates to other species, or allelic variants, of the sole described "human" GDNF polynucleotide encoding the polypeptide of SEQ ID NO:2. Analogous to the situation decided in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), "an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". *Fiddes v. Baird*, 30 USPQ2d 1481, 1483 (1993) held that claims

directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class, in which the specification had provided an adequate description of only the bovine sequence. Similarly, only the single human polynucleotide encoding the polypeptide species of SEQ ID NO:2 has been described in the instant specification.

Accordingly, as it relates to the required components necessary to practice the claimed method, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, an invitation for others to discover a representative number of species with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics has not reasonably been provided within the instant specification. Thus, Applicant was not reasonably in possession of the claimed genus of GDNF polynucleotides at the

time of filing the instant application, in which no assayable function is further recited for discovering other members of the claimed genus.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999. (See Examples 11, 13 & 17).

7. Claims 31 & 45 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing survival of dopaminergic neurons with structurally defined GDNF polypeptides, does not reasonably provide enablement for any *in vivo* method for promoting some unknown and undescribed function within dopaminergic neurons using gene therapy; especially as it relates to using structurally and functional uncharacterized polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues on pages 6-9 of the response that "Applicants have provided sufficient evidence to rebut the Examiner's allegation that the claimed methods to increase survival of dopaminergic neurons are not enabled by the present invention", references Bohn et al. (1997) and cites *In re Marzocchi, In re Borkowski* and *Ex parte Nardi.* In contrast to Applicant's assertions, the claims still fail to recite distinguishable functional characteristics for the variants claimed, which alternatively encompass random mutations that one skilled in the art would

predict to result in inactive polynucleotide molecules. Second, the claims are not limited to "increas[ing] survival of dopaminergic neurons", but recite "promoting the [unknown and undefined] ... *function* of dopaminergic neurons...", which alternatively still encompass regeneration of dopaminergic cells that does not occur; consistent with the teaching of Jackowski previously made of record. Third, Bohn et al (1997) is published 2 years after the claimed priority date, and importantly describes a specific replication-defective adenoviral vector containing GDNF (which alternatively is not described in the instant specification), that is "injected... [the Ad vector construct] immediately dorsal into the striatum" (pg. 839 (1st column)), so that "delivery can be located near degenerating neuronal soma or target neurons", in order to "likely minimize deleterious side effects that may result from exposure of other cells to excess GDNF"..., but wherein "stable transgene expression in the Parkinsonian brain may be achieved *in the future* through the use of *new generation Ad vectors*"[emphasis added] (pg. 840, 3rd col.). Additionally, in contrast to Applicant's assertions, a *prima facie* case for lack of enablement has clearly been established in the previous Office action, in which Applicant interestingly has not commented on the teachings from the governing body (NIH) for conducting gene therapy (i.e., the 1995 "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" which again states that:

"While the expectations and the promise of gene therapy are great, clinical efficacy has not been definitely demonstrated at this time in *any gene therapy protocol*, despite anecdotal claims of successful therapy and the initiation of more than 100 Recombinant DNA Advisory Committee (RAC)-approved protocols.

Significant problems remain in all basis aspects of gene therapy. Major difficulties at the basic level include *shortcomings in all current gene transfer vectors* and an *inadequate understanding of the biological interaction of these vectors with the host"* [emphasis added; page 1].

Thus, Applicant's arguments are not on point, and therefore, are not persuasive for the reasons made of record.

8. Claims 31 & 45 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds envisioned by the recitation "function of neurons" to be "affected" remain unknown since it is unknown if increasing or decreasing a particular assayable function is envisioned, or even what exact "function" to be "affected" is intended; thereby, still being indefinite.

9. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 45 is now dependent on cancelled claim 32.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
November 18, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600